JAMA Clinical Guidelines Synopsis

# Management of Acute Coronary Syndrome

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**GUIDELINE TITLE** ACC/AHA/ACEP/NAEMSP/SCAI Guideline for the Management of Patients With Acute Coronary Syndrome

**RELEASE DATE** February 27, 2025

**PRIOR VERSIONS** 2013 and 2014

**DEVELOPERS** American College of Cardiology (ACC), American Heart Association (AHA), American College of Emergency Physicians (ACEP), National Association of EMS Physicians (NAEMSP), and Society for Cardiovascular Angiography and Interventions (SCAI)

**FUNDING SOURCE** ACC and AHA

**TARGET POPULATION** Patients with acute coronary syndrome (ACS)

**SELECTED RECOMMENDATIONS**

- All patients with ACS should receive loading doses of aspirin (162-325 mg) and a P2Y12 inhibitor (strength of recommendation [SOR]: 1; quality of evidence [QOE]: A). Aspirin and P2Y12 inhibitor maintenance therapy should be continued for at least 1 year for individuals not at high risk of bleeding (SOR: 1; QOE: A). Ticagrelor or prasugrel are recommended over clopidogrel for patients with non–ST-elevation ACS (SOR: 1; QOE: B). For patients who require oral anticoagulation, aspirin should be discontinued after 1 to 4 weeks (SOR: 1; QOE: B).
- High-intensity statins are recommended to reduce risk of major adverse cardiovascular events (MACE) (SOR: 1; QOE: A). For patients taking maximally tolerated statin therapy with low-density lipoprotein cholesterol (LDL-C) of 70 mg/dL or higher, adding a nonstatin lipid-lowering agent is recommended (SOR: 1; QOE: A).
- For patients with non–ST-elevation ACS at intermediate to high risk of ischemic events, an invasive approach with intent for revascularization is recommended during hospitalization (SOR: 1; QOE: A).
- For patients undergoing invasive coronary angiography, a radial approach is recommended over a femoral approach (SOR: 1; QOE: A).
- For patients with ST-elevation myocardial infarction (STEMI) and multivessel coronary disease (SOR: 1; QOE: A), complete revascularization, which involves percutaneous coronary intervention (PCI) of culprit and significant nonculprit coronary artery lesions, is recommended to reduce risk of MACE.

## Summary of the Clinical Problem

In the US, more than 800 000 acute myocardial infarctions (MIs) occur annually.[1] Since publication of the 2013 ACC Foundation/AHA guideline on STEMI and the 2014 AHA/ACC non-STEMI guideline, there have been substantial advances in pharmacological and invasive treatment of ACS. This summary focuses on recommendations about medication management and revascularization for patients with ACS.

Supplemental content

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## Characteristics of the Guideline Source

The guideline[1] was developed without commercial support by selected experts in cardiology, cardiovascular surgery, emergency medicine, advanced practice nursing, and clinical pharmacy as well as patient representatives. Of the 30-member committee, 19 members (including the chair) had no relevant conflicts of interest (eTable in the Supplement).

## Evidence Base

Strength of recommendation was rated from 1 (strong) to 3 (no benefit or harm) based on the balance of benefits and risks. Quality of evidence was rated as A to C, with A evidence supported by high-quality randomized clinical trials (RCTs), meta-analyses, or at least 1 RCT corroborated by high-quality registry studies.[1] In total, 103 recommendations were made; 63 had an SOR of 1, of which 25 were supported by a QOE of A and 16 supported by a QOE of B from RCTs.

### Medical Management

Dual antiplatelet therapy for at least 1 year for individuals not at high risk of bleeding is first-line medical management of ACS. In an RCT of 12 562 patients presenting with non–ST-elevation ACS within 24 hours of symptom onset, patients receiving a 300-mg loading dose of clopidogrel followed by 75 mg/d in addition to aspirin (75-325 mg/d) had reduced risk of composite cardiovascular death, nonfatal MI, and stroke vs those receiving aspirin alone (9.3% vs 11.4%; respectively; relative risk, 0.80; 95% CI, 0.72-0.90; $P < .001$).[2] Compared with clopidogrel, more potent P2Y12 inhibitors such as prasugrel and ticagrelor further decrease risk of MACE. In an RCT of 13 608 patients with ACS scheduled for PCI and randomized within 72 hours of symptoms to receive prasugrel or clopidogrel, prasugrel resulted in fewer composite cardiovascular deaths, nonfatal MIs, and strokes vs clopidogrel (9.9% vs 12.1%; hazard ratio [HR], 0.81; 95% CI, 0.73-0.90; $P < .001$).[3] However, major bleeding events occurred more frequently with prasugrel than clopidogrel (2.4% vs 1.8%; HR, 1.32; 95% CI, 1.03-1.68; $P = .03$), including fatal bleeding (0.4% vs 0.1%; HR, 4.19; 95% CI, 1.58-11.11; $P = .002$).[3] Patients with a previous stroke or transient ischemic attack had net harm from prasugrel vs clopidogrel (23% vs 16%; HR, 1.54; 95% CI, 1.02-2.32; $P = .04$); these conditions are absolute contraindications for prasugrel use. Relative contraindications include age 75 years or older and weight less than



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60 kg due to lack of net clinical benefit, defined as rate of all-cause death, nonfatal MI, nonfatal stroke, and non–coronary artery bypass grafting–related nonfatal thrombolysis in MI major bleeding. Similarly, in an RCT of 18 624 patients hospitalized with unstable angina, non-STEMI, or STEMI, those receiving ticagrelor had decreased risk of composite death due to vascular causes, MI, and stroke vs clopidogrel (9.8% vs 11.7%; HR, 0.84; 95% CI, 0.77-0.92; *P* < .001); however, no difference was observed in major bleeding (11.6% vs 11.2%; HR, 1.04; 95% CI, 0.95-1.13; *P* = .43) or fatal bleeding (0.3% vs 0.3%; HR, 0.87; 95% CI, 0.48-1.59; *P* = .66).[4]

For patients with ACS who require oral anticoagulation, discontinuation of aspirin after 1 to 4 weeks is recommended. In a 2 × 2 factorial design trial of 4614 patients randomized to either apixaban or a vitamin K antagonist (open label) and aspirin or matching placebo (double blind) for 6 months, major bleeding was higher among patients randomized to aspirin than placebo (16.1% vs 9.0%; HR, 1.89; 95% CI, 1.59-2.24; *P* < .001) without an increase in ischemic events.[5]

High-intensity statin and nonstatin lipid-lowering medications are recommended to reduce the rate of cardiovascular events. In an RCT of 4162 patients hospitalized for ACS in the preceding 10 days, those receiving 80-mg atorvastatin had decreased risk of composite death due to any cause, MI, unstable angina requiring hospitalization, revascularization, and stroke vs those receiving 40-mg pravastatin (22.4% vs 26.3%; HR, 0.84; 95% CI, 0.74-0.95; *P* = .005) at a mean 24-month follow-up.[6] In a substudy of 1949 patients who had LDL-C measured at 4 months, those with LDL-C of 40 mg/dL or lower or between 40 and 60 mg/dL had fewer MACE (20.4% in each group) vs those with LDL-C between 80 and 100 mg/dL (26.1%) (multivariable-adjusted HRs, 0.61 [95% CI, 0.40-0.91] and 0.67 [95% CI, 0.50-0.92], respectively).[7] Multiple studies have reported a decreased risk of atherosclerotic cardiovascular disease outcomes with use of nonstatin lipid-lowering therapies, including ezetimibe, monoclonal antibodies to proprotein convertase subtilisin/kexin type 9 (eg, alirocumab and evolocumab), and bempedoic acid. These medications are recommended for patients with ACS taking maximally tolerated statin therapy who have LDL-C of 70 mg/dL or greater or for those with statin intolerance.[1]

### Revascularization

Cardiac catheterization with an intent to revascularize is recommended for patients with non-STEMI ACS who are at intermediate to high risk of ischemic events based on well-validated risk scores (eg, GRACE risk score >109). An RCT of 2220 patients reported that those randomized to routine cardiac catheterization within 48 hours had lower rates of composite death, nonfatal MI, and rehospitalization for ACS at 6 months vs those randomized to catheterization only if there was objective evidence of recurrent ischemia or an abnormal stress test result (15.9% vs 19.4%; odds ratio, 0.78; 95% CI, 0.62-0.97; *P* = .03).[8]

Among patients with ACS undergoing PCI, a radial approach is preferred over a femoral approach. In a meta-analysis of 7 RCTs including 21 600 patients undergoing an invasive approach, radial artery access had lower rates of all-cause 30-day mortality (1.6% vs 2.1%; HR, 0.77; 95% CI, 0.63-0.95; *P* = .01) and major bleeding (1.5% vs 2.7%; odds ratio, 0.55; 95% CI, 0.45-0.67; *P* < .001) compared with femoral access.[9]

Complete revascularization for STEMI has been evaluated in multiple RCTs. An RCT of 4041 patients with STEMI and multivessel disease who had undergone successful PCI of culprit lesions randomized these patients to PCI of angiographically significant nonculprit vessels (complete revascularization) or no further intervention. Complete revascularization reduced composite cardiovascular death and MI (7.8% vs 10.5%; HR, 0.74; 95% CI, 0.60-0.91; *P* = .004).[10]

## Discussion

The 2025 ACS guideline recommends medical therapy with a loading dose of both aspirin and a P2Y12 inhibitor followed by maintenance dual antiplatelet therapy and invasive management with PCI. There are new recommendations for early discontinuation of aspirin for patients requiring anticoagulation. The guideline incorporates new evidence to lower bleeding risk in patients requiring dual antiplatelet therapy after PCI for ACS by suggesting that it is reasonable to switch dual antiplatelet therapy from prasugrel or ticagrelor to clopidogrel after 1 month (SOR: 2; LOE: B) and to lower ischemic risk of stent placement in the left main artery or complex lesions by using intravascular imaging (SOR: 1; LOE: A). Although complete revascularization is recommended for both patients with STEMI and patients with non-STEMI, uncertainty remains about its use in patients with non-STEMI. Results from ongoing RCTs investigating complete revascularization in patients with non-STEMI and multivessel disease may inform future practice.


## ARTICLE INFORMATION

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